



427.047

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: : M. Meller  
MICHEL AUGUET et al :  
Serial No.: 09/937,306 : Group: 1654  
Filed: September 20, 2001 :  
For: COMBINATION...ANTIOXIDANT(S):  
475 Park Avenue South  
New York, N.Y. 10016  
April 8, 2004

RESPONSE

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Responsive to the office action of December 1, 2003, Applicants request  
reconsideration of the application in view of the remarks presented herein.

The claims in the application are claims 1, 4 to 12, 25 and 36. Claims 25 to 36  
have been withdrawn from consideration.

Claims 1 and 4 to 12 were rejected under 35 USC 102 as being anticipated by the  
Naftchi et al '933 or '962 patents. The Examiner maintains the rejections since it is  
clearly shown in the cited portions of the patents they teach both ingredients together  
lipioc acid and aminoguanidine and the claims are drawn to a composition consisting  
essentially of a NO synthase inhibitory substance and a metabolic antioxidant substance  
which the two references teach.

Applicants vigorously these grounds of rejection since the Naftchi et al patents neither anticipate nor render obvious Applicants' invention. The Examiner has cited column 133 of the '933 patent and column 119 of the '962 patent. Neither one of these portions of the patents teach Applicants' compositions which are a two-component composition comprising a pharmaceutical consisting essentially of two active ingredients, 1) a NO synthase inhibitory substance and 2) a metabolic antioxidant substance possessing at least two thio groups and which intervenes in the redox status of thio groups and optionally, a pharmaceutically acceptable support with the composition having a dual activity of inhibiting NO synthase and an antioxidant activity.

It is clear that the Naftchi et al patents do not relate to a mixture of an NO synthase inhibitory substance and a metabolic antioxidant substance but, rather, to a reactant of two such compounds. In column 119 of the '962 patent, there is a reaction between  $\alpha$ -lipoic acid and aminoguanidine to form compound No. 208 of Table 1, namely, N-(1,2-dithiolane-3-3-pentanamido)-guanidine. This has the structure of the compound indicated as compound 208 in Table 1 in columns 89 and 90. It is clear that this is a single compound as a result of the reaction of the two ingredients. In contrast thereto, Applicant s' compositions are drawn to two discrete different activities and not to a reactant of the two ingredients. Therefore, the Naftchi et al patent neither anticipates nor renders obvious Applicants' invention. Moreover, it does not teach Applicants' NO synthase activity or antioxidant activity. Therefore, this ground of rejection clearly fails and withdrawal of the same is requested.


Claims 1 and 4 to 12 were rejected under 35 USC 103 as being obvious over the Naftchi et al patents or the Petrus or Lai patents. The Examiner indicates that the Petrus and Lai patents teach in columns 3 and 4 and columns 12 and 21, respectively, that the references contain the claimed ingredients together and therefore, they would be obvious.

Applicants respectfully traverse these grounds of rejection since the individual references do not render obvious Applicants' invention. The Naftchi et al patents are clearly related to a different invention as pointed out above with respect to the 102 rejection. The Lai patent relates to a conjugate of nitrogen oxide scavengers and dithiocarbamates and by conjugates, this means a reactant derived from the same which has the same deficiency as noted above for the Naftchi et al patents. The Petrus patent relates to a method of treating arthritis by administering a composition comprising an inhibitor of nitric oxide synthase and an amino sugar and this is not the same as an antioxidant. Therefore, this has nothing to do with Applicants' invention since the amino sugars are "the building blocks of articular cartilage and have anti-inflammatory actions" (see lines 48 and 49 of column 2). This is a completely different activity. The Lai patent relates to a compound comprising a dithiocarbamate containing nitrogen oxide scavenger attached by a covalent bond to a pharmacologically active agent which is useful for treating a pathological condition. Applicants' compositions are in no way taught by the said references and Applicants' compositions are directed to compositions and not to compounds derived from the reaction of two separate compounds.

It should be noted that there is no relation between the NO synthase inhibition as described in Applicants' invention and the  $\alpha$ -adrenergic activity described in the Naftchi et al patents. The teaching of the latter patents cannot suggest a combination of a NO synthase inhibitor with a second therapeutic agent useful as an antioxidant. Therefore, there is no suggestion whatsoever of Applicants' invention from the prior art cited by the Examiner. Therefore, these grounds of rejection fail and withdrawal of the same is requested.

In view of the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,  
Muserlian, Lucas and Mercanti

  
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CAM:ds  
Enclosure